REMARKS

Claims 1-12, 15-34, 37, 43-47, 50-54, 56-58, 60, 61, 63-77, and 97-102 are pending. Among them, Claims 7 and 75-77 are withdrawn as directed to non-elected inventions.

Applicants thank the Examiner for accepting the drawings submitted on Nov. 8, 2008.

Applicants respectfully request reconsideration of the amended claims in view of the following remarks.

Application Status

In the Office Action Summary page, both the "This action is **Final**" and the "This action is non-Final" boxes are checked. This Action should be non-Final, because (1) there are new grounds of rejection not necessitated by Applicants' amendments or IDS citation; (2) the Examiner does not state that this action is made Final in the text of the Office Action; and (3) the USPTO public PAIR indicates that the current status of this application is "Non-Final Action Mailed" in the Application Data tab.

Nevertheless, Applicants' attorney Yu Lu called the Examiner on July 21, 2008 to clarify the application status. The Examiner returned the call on the same day, and indicated that this is indeed a non-Final Office Action. In case this call is considered an Interview with the Examiner, this response also constitutes the substantive statement required under 37 C.F.R. § 1.133(b).

Claim Objections

Applicants thank the Examiner for withdrawing the objection to Claims 1, 43, 44, 47, 60, 67, and 102 in view of Applicants' amendments.

Regarding Claim 31, the Examiner suggests that Applicants further clarify the language of the claim in view of Applicants' previous argument. Although Applicants believe that the original language is clear, Applicants have adopted the Examiner's suggestion in order to advance prosecution. The amendment does not change the scope of Claim 31. It merely clarifies the claim. Reconsideration and withdrawal of the objection are respectfully requested.

Claim rejection under 35 U.S.C. § 102

Claims 1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97, and 99 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Evans *et al.* (US 2002/0177564, or "Evans").

In making the rejection, the Examiner broadly interprets the term "recombinant polymerase III promoter" as a promoter comprising any portion of a pol III promoter in combination with elements from other promoters, presumably such that the combination artificial promoter would work to transcribe DNA. The Examiner appears to argue that the specification adopts a broad definition of the promoter by defining the recombinant pol III promoter as including a promoter comprising a TATA box. As a result, the Examiner argues that the claimed recombinant polymerase III promoter could be viewed to read on some of the Pol II promoters purportedly recited in Evans.

Although Applicants disagree with the Examiner's unreasonably broad interpretation, solely to advance prosecution, Applicants have amended independent Claim 1 to explicitly require that the RNA polymerase III promoter must be able to use RNA Polymerase III for transcription. This amendment does not narrow the scope of the claims. It merely clarifies their original intended meaning.

It is appreciated that the Examiner's rejection appears premised on her interpretation that the specification lacks any functional definition limiting "pol III promoter" to one that can be used by RNA polymerase III. Applicants however respectively suggest that such a functional definition is implicit in the art recognized understanding of the term. Moreover, explicit and implicit support conforming to such an art recognized understanding may be found throughout the specification, *see*, for example, the last paragraph of page 2, where the specification explicitly states that "[i]n some aspects, the invention provides a system for the regulated expression of an RNA molecule. In some aspects, the invention provides systems for expressing double-stranded or hairpin RNA molecules transcribed by RNA polymerase III under inducible, tissue specific, developmental, temporal or other modes of regulation" (emphasis added).

In addition, the instant specification describes that the recombinant Pol III promoter is to

be used by RNA Polymerase III. For example, Example 1 uses the U6 promoter, which as was recognized in the art, is a promoter that can be used by RNA polymerase III. Also *see* page 10, last paragraph, reciting "a modified polymerase III specific U6 promoter" (emphasis added). Page 18, first paragraph, when describing the transcription factor that regulates the activity of the subject Pol III promoter, likewise states that "[i]n some embodiments, the transactivation domain preferentially promotes transcription of polymerase III over that of polymerase I or polymerase II. Accordingly, in preferred embodiments, the transactivation domain is polymerase III specific" (emphasis added).

As amended, Claim 1 clearly states a functional relationship between the RNA Pol III promoter and RNA Pol III. In contrast, as argued in the previous response, Evans fails to disclose a recombinant polymerase III promoter that can be used by RNA polymerase III, and thus cannot anticipate the claimed invention.

Specifically, Evans recites the use of a recombinant Pol II promoter for expressing exogenous gene or cDNA in a mammalian host. The recombinant Pol II promoter "comprise at least a minimal promoter in combination with an ecdysone response element. A minimal promoter, when combined with an enhancer region (e.g., a hormone response element), functions to initiate mRNA transcription in response to a ligand/receptor complex." See paragraph **[0165]** of Evans, and also Figure 2 of Evans. Evans itself lists many Pol II promoters said to be suitable for its constructs (see paragraph **[0170]**), including an explicit recitation of "RNA Pol II promoter." Conspicuously missing is any reference to "RNA Pol III promoter," which is used for transcription of a limited number of genes that synthesize ribosomal 5S rRNA, tRNA, and other small RNAs, but not mRNA encoding proteins.

Therefore, the weight of the evidence favors Applicants' assertion that Evans fails to teach or suggest any recombinant polymerase III promoter that can be used by RNA polymerase III, and the Examiner has not provided any scientific reasoning or reference that tends to prove the contrary. Thus Evans does not anticipate the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Claims 1-4, 11, 25, 28-31, 33, 34, 37, 43, 50-52, **53**, 56, 58, 60, 63-73, 98, and 99 stand

rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Li *et al.* (US 2004/0146858, or "Li"). The Examiner argues that Li teaches an RNA Pol III promoter (a mammalian U6 promoter) operably connected to a tetO site, and that "a tet repressor is under expression of an inducible promoter." The Examiner further argues that "Claim 31 alones [sic] limits the activity of the transcription factor to be one that increases transcription from the recombinant RNA polymerase promoter. Absent the limitation in claim 31, claim 1 is open to interpretation that the transcription factor activates and represses expression."

Applicants disagree. As amended, Claim 1 already recites "wherein the transcription factor increases transcription ..." (emphasis added). Therefore, contrary to the Examiner's assertion, Claim 1 is not open to interpretation that the transcription factor *activates and represses* expression.

Reconsideration and and withdrawal of the 35 U.S.C. § 102 rejections are respectfully requested.

Claim rejection under 35 U.S.C. § 103(a)

Claim 46 stands rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Evans (of record) as applied to Claims 1, 2, 4, 8-12, 15-22, 25-33, 37, 43-45, 47, 50, 57, 58, 60, 61, 63-74, 97, and 99 above, and further in view of Cheng *et al.* (*Gene Therapy* 4: 1013-1022, 1997). The Examiner argues that Evens fails to teach the use of GFP as a reporter, but she asserts that Cheng allegedly makes up this deficiency.

As described above, Applicants have amended Claim 1 to explicitly clarify the functional relationship between the RNA Pol III promoter and RNA Pol III. Thus Evans and Cheng, even if combined, do not teach all the limitations of the claims.

The Examiner also newly rejects Claims 54 and 100-102 under 35 U.S.C. 103(a) as allegedly being unpatentable over Evans (or record) or Li (of record) further in view of Gardner *et al.* (U.S. Pat. No. 6,841, 376).

Regarding Claim 54, the Examiner acknowledges that Evans and Li fail to teach an expression system used to express a ribozyme, but argues that Gardner makes up the deficiency.

For the same reasons explained above, Gardner fails to remedy the deficiency in Evans and Li due to the clarifying amendment to Claim 1. Reconsideration and withdrawal of this rejection are respectfully requested.

Regarding Claims 100-102, the Examiner argues that Gardner contains disclosure (e.g., Figure 3b) that satisfy the missing elements in Evans and Li. Applicants respectfully disagree.

Specifically, Gardner recites a reciprocal double negative feedback inhibition system (see Figures 1-4), wherein the expression product (R1) of the first transcription unit is a transcription repressor for the promoter (P2) of the second transcription unit, while the expression product (R2) of the second transcription unit is in turn a transcription repressor for the promoter (P1) of the first transcription unit. Neither R1 nor R2 increases transcription from any promoter, let along RNA Pol III promoter, as recited in Claim 1. Thus Gardner cannot cure the deficiency of Evans and Li. Reconsideration and withdrawal of the obviousness rejection are respectfully requested.

CONCLUSIONS

Applicants believe no fee in addition to those listed in the accompanying amendment transmittal (filed concurrently herewith) is due with this response. However, if any other fee is due, please charge our Deposit Account No. **18-1945**, from which the undersigned is authorized to draw under Order No. **CSHL-P01-012**.

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Respectfully submitted,

By_____

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